REMARKS

Amendments to the Specification

Applicants have amended the first paragraph of the specification to delete the claim to priority to the Czechoslovakian patent application PV-709-92 (filed March 11, 1992). The reason for that amendment is explained below under the subheading "Claim to Priority. . . ."

Amendments to the Claims

Independent Claims 22, 30 and 42 have been amended to point out with more particularity and clarity the subject matter regarded by the Applicants as their invention. The independent claims have been amended to specify that the claimed anti-idiotype antibody "comprises an internal image **corresponding to an epitope**" of an MN protein or of an MN polypeptide, "wherein said MN protein is encoded by a nucleic acid selected from the group consisting of (a) SEQ ID NO: 1; and (b) polynucleotides that differ from SEQ ID NO: 1 due to the degeneracy of the genetic code . . . " [claim 22 as amended], or

> wherein said MN polypeptide is encoded by a nucleic acid that comprises a polynucleotide containing at least 25 nucleotides, said nucleic acid being selected from the group consisting of:
>
> (a) SEQ ID NO: 1; and

(b) polynucleotides that differ from SEQ ID NO NO: 1 due to the degeneracy of the genetic code.

[Claim 42 as amended.]

The phrase "**corresponds to an epitope of an MN protein/polypeptide**" has been defined in the Specification, and has been added to the independent claims to specify that the anti-idiotype antibodies comprise functional mimics of MN protein epitopes, that confer protective immunity and/or anti-tumorigenic activity when administered as a vaccine.

> **The term "corresponding to an epitope of an MN protein/polypeptide"** will be understood to include the practical possibility that, in some instances, **amino acid sequence variations of a naturally occurring protein or polypeptide may be antigenic and confer protective immunity against neoplastic disease and/or anti-tumorigenic effects**. Possible sequence variations include, without limitation, amino acid substitutions, extensions, deletions, truncations, interpolations and combinations thereof. **Such variations fall within the contemplated scope of the invention provided the protein or polypeptide containing them is immunogenic and antibodies elicited by such a polypeptide or protein cross-react with naturally occurring MN proteins and polypeptides to a sufficient extent to provide protective immunity and/or anti-tumorigenic activity when administered as a vaccine**.

[Instant specification, page 82, lines 11-21; emphasis added.]

The Specification clearly indicates that the claimed anti-idiotype antibodies are functional mimics of MN proteins/polypeptides. For example at page 13, lines 12-17, the instant Specification states:

> Disclosed herein are biologically active MN proteins and MN polypeptides that are useful as vaccines to protect vertebrates, preferably mammals, more preferably humans, against neoplastic diseases associated with abnormal MN expression. Such vaccines are also useful to boost a patient's immunity to such a disease. **Such vaccines can alternatively comprise an anti-idiotype MN-specific antibody.**

[Emphasis added.] Another such example can be found in the Specification at page 75, lines 20-25 which reads:

> Uemura et al., Biotherapy (Japan) 10(3): 241-244 (1996) (English summary) define an **anti-idiotype antibody (Ab2)** as "an antibody directed against an antigenic determinant located within a variable region of the immunoglobulin molecule. **Ab2 mimicking the normal antigen (so-called internal image Ab2) may be used as a surrogate antigen for vaccination to trigger the host's immune system** specifically against the nominal antigen."

[Emphasis added.]

The independent claims 22, 30 and 42 have been further amended for particularity and clarity by eliminating original subclaim (b), as well as the phrase in original subclaim (c) that refers to original subclaim (b). Those subclaim amendments

were made to point out with more particularity and clarity the subject matter regarded by the Applicants as their invention in view of the above-discussed amendment to each of the independent claims, which amendment adds the phrase "wherein said anti-idiotype antibody comprises an internal image corresponding to an epitope of said MN protein. . . " or ". . . to said MN polypeptide. . . ."

Applicants respectfully conclude that no new matter has been entered by the above amendments. Claims 22-23, 30-31, 36-38, 42-43 and 46-48 are now pending and under examination. Applicants respectfully request entry of the above amendments and reconsideration and allowance of the claims as amended.

New Grounds of Rejection (Sections 4 and 15 of Final Office Action)

The Examiner indicates at page 2 (section 4) and at page 16 (section 5) that the Final Office Action contains new grounds of rejection. Applicants respectfully request clarification and identification of the new grounds of rejection.

35 U.S.C. Section 112, First Paragraph Rejection (Section 10 of Final Office Action)

Claims 22-23, 30-31, 36-38, 42-43 and 46-48 stand rejected under 35 U.S.C. Section 112, first paragraph, because "the specification does not enable any person skilled in the relevant art to which it pertains . . . to make or use the invention commensurate in scope with the claims. . . ." [Final Office Action, Section 10, page 3.] Applicants respectfully submit that the amendments to the independent claims meet and overcome the subject rejection.

Applicants respectfully point out that independent Claims 22, 30 and 42 have been amended to indicate that the claimed anti-idiotype antibody "comprises an internal image corresponding to an epitope" of an MN protein or an MN polypeptide, "wherein said MN protein is encoded by a nucleic acid selected from the group consisting of (a) SEQ ID NO: 1; and (b) polynucleotides that differ from SEQ ID NO: 1 due to the degeneracy of the genetic code . . . " [claim 22 as amended], or

> wherein said MN polypeptide is encoded by a nucleic acid that comprises a polynucleotide containing at least 25 nucleotides, said nucleic acid being selected from the group consisting of:
>
> (a) SEQ ID NO: 1; and

(b) polynucleotides that differ from SEQ ID NO NO: 1 due to the degeneracy of the genetic code.

[Claim 42 as amended.]

As indicated above under the REMARKS, the phrase "corresponding to an epitope" of an MN protein or an MN polypeptide has a specific meaning as defined by the instant specification, to mean that the anti-idiotype antibody comprises an immunogenic functional mimic of an MN protein epitope. The phrase "comprises an internal image corresponding to an epitope of an MN protein/polypeptide" then means that the claimed anti-idiotype antibody is immunogenic, and that antibodies elicited by the claimed anti-idiotype antibody "**cross-react with naturally occurring MN proteins and polypeptides to a sufficient extent to provide protective immunity and/or anti-tumorigenic activity when administered as a vaccine**." [Instant specification, page 82, lines 19-21; emphasis added.]

As indicated above under the REMARKS, the Specification clearly indicates that the anti-idiotype antibodies of Applicants' invention are functional mimics of MN proteins/polypeptides. The independent claims as amended set forth that attribute of functional mimicry with particularity and clarity and address the Examiner's concern that the previous wording of the independent claims could encompass "anti-

idiotypic antibodies [that] would not express three-dimensional shapes that resemble the structure of the natural MN antigen." [Final Office Action, page 4.] As amended, Claims 22, 30 and 42 clearly refer only to anti-idiotype antibodies that mimic the linear or conformational epitopes of the native MN protein/polypeptides.

Applicants respectfully conclude that the above amendments to the independent claims 22, 30 and 42 meet and overcome the subject rejection. Applicants respectfully request that the Examiner reconsider and withdraw this rejection in view of the above amendments and remarks.

Claim to Priority (Page 10 of Office Action)

The Office Action states at page 10 that the "Czechoslovakian Patent application PV-709-92 discloses the M75 monoclonal antibody secreted from the hybridoma VU-M75. This does not provide adequate descriptive support for the instantly claimed invention, which is drawn to anti-idiotypic antibodies that mimic the MN protein." Applicants respectfully point out that those statements are consistent with the Applicants' position that without possession of the M75 monoclonal antibody or another MN-specific antibody, and/or the MN amino acid or cDNA sequence, one of skill in the art would not be able to make

reproducibly a MN-specific antibody, and would have no idea how to make the claimed anti-idiotype antibodies comprising an internal image corresponding to an MN protein/polypeptide epitope.

Applicants respectfully point out that analogously none of the prior art references cited in the Office Action, notably neither Pastorekova et al. nor Oosterwijk et al. (WO 88/08854) nor Oosterwijk et al. (1986), disclose how to produce an MN-specific antibody reproducibly, let alone the claimed anti-idiotype antibodies, nor do such prior art references characterize or provide the MN amino acid sequence or MN cDNA sequence. The Czechoslovakian patent application PV-709-92 basically discloses at least as much information about the M75 Mab as does Pastorekova et al.

Applicants respectfully withdraw priority from the Czechoslovakian patent application PV-709-92, as indicated above in the amendment to the instant specification.

35 U.S.C. Section 103 Rejections (Sections 11-13 of Office Action)

Applicants gratefully again acknowledge the March 7, 2005 telephone interview with Examiners Larry Helms and David Blanchard. Applicants respectfully also again point out that

the phrase "publicly available" as used in the Final Office Action was discussed in that telephone interview, and that the Examiners informed the Applicants that that phrase was not equivalent to that of "public use" in 35 U.S.C. §102(b), but was used in that the Examiners had assumed that the hybridioma which secretes the G250 Mab had been deposited in an international depository at the time of the publication of the cited prior art references. Applicants appreciated the Examiners' attention to and consideration of Applicants' information provided during the interview, regarding the lack of such a deposit of the G250 hybridoma, the lack of enablement to produce the G250 Mab or any MN-specific antibody reproducibly, and the absence of any information or characterization concerning the MN protein or MN cDNA at the earliest U.S. priority date claimed for the instant application, that is, October 21, 1992.

First 35 U.S.C. § 103(a) (Section 11 of Final Office Action)

Claims 22-23, 30-31, 36-38, 42-43 and 46-48 stand "rejected under 35 U.S.C. 103(a) as being unpatentable over Pastorekova et al [Virology 187:620-626, 1992] as evidenced by Pastorek et al [Oncogene 9:2877-2888, 1994] in view of Raychaudhuri et al [J. Immunology 137:1743-1749, 1986]." [Office Action, page 11, Section 11.] Applicants respectfully rely on

the arguments and facts made of record in the prosecution of the instantly claimed invention, as those presented in the response to the first office action submitted to the PTO on July 22, 2004, to show that no prior art references disclosed how to make reproducibly the M75 Mab or any MN-specific antibody prior to the disclosure of the earliest U.S. priority application for the instant application, nor did any prior references characterize the MN protein or provide the MN amino acid sequence or the MN cDNA sequence before the earliest U.S. priority date claimed for the instant application. Applicants further respectfully suggest that the arguments and facts of record will clearly and sharply announce the non-obviousness of the instantly claimed invention, once the misconception under which the Examiners had been analyzing the claimed invention, that is, that the G250 antigen had been characterized and that the G250 hybridoma had been deposited, is removed.

Applicants respectfully expect that the arguments and facts of record conclusively establish the novelty and non-obviousness of the claimed invention. However, Applicants are willing to go further in the instant U.S. prosecution to establish absolutely that the instant rejection cannot stand by pointing out that Pastorekova et al. (1992) cannot be cited against the instant claims with priority to October 21, 1992,

because Pastorekova et al. (1992) was published less than a year before the claimed priority date. Without Pastorekova et al. (1992), the instant rejection must fall because Raychaudhari et al. provides no information whatsoever about the MN protein, MN cDNA, MN-specific antibodies, and certainly makes no suggestion concerning the instantly claimed anti-idiotype antibodies comprising an internal image corresponding to an MN protein/polypeptide epitope. Pastorek et al. (1994) cannot be used in combination with Raychaudhuri since Pastorek et al. (1994) is not a prior art reference, having been published about two years after the instant application's earliest U.S. priority date.

An inventor's own prior work cannot be cited against him or her, in the absence of a statutory bar[1]. The Pastorekova et al. reference cannot be cited against the Applicants, as it was published less than one year before the earliest priority date of the instant invention (that is October 21, 1992), has the same inventive entity as the instant application and the priority application, and **does not constitute a statutory bar**. As 35 U.S.C. 102 reads in pertinent part:

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1. Riverwood International Corp. v. R.A. Jones & Co., 324 F.3d 1346, 1355, 66 USPQ2d 1331 (Fed. Cir. 2003) ["One's own work may not be considered prior art in the absence of a statutory basis. . . ."]. See Chisum §5.03[3][f].

> A person shall be entitled to a patent unless -
>
> . . . .
>
> (b) the invention was . . . described in a printed publication in this or in a foreign country . . . more than one year prior to the date of the application for patent in the United States. . . .

Applicants respectfully submit that they are the same inventive entity as that of the priority application No. 07/964,589 (now US Patent 5,387,676) filed October 21, 1992, and further, that with respect to the inventive subject matter of the instant application relating to the M75 monoclonal antibody, Applicants are the same inventive entity as that of Pastorekova et al., published April 1992, less than one year before the earliest U.S. priority date of the instant invention. In support of Applicants' assertion that they are the same inventive entity as that of Pastorekova et al. 1992, enclosed herewith are two Declarations under MPEP 715(c) [Appendices 1 and 2].

Appendix 1 contains an affidavit signed by the three authors of Pastorekova et al. 1992 not listed as inventors in the instant application [Dr. Zuzana Zavadova, Dr. Michael Kostal and Olga Babusikova] to the effect that Dr. Jaromir Pastorek, Dr. Jan Zavada and Dr. Silvia Pastorekova are the sole inventors

of the subject matter of priority application No. 07/964,589 [the '676 patent.] Appendix 2 is an affidavit by the three inventors of the instant invention [Dr. Jaromir Pastorek, Dr. Jan Zavada and Dr. Silvia Pastorekova] asserting that Dr. Jaromir Pastorek was involved in the conception and reduction to practice of the inventive subject matter of the same priority application No. 07/964,589. With respect to the subject matter regarding the M75 Mab in the instant invention, Applicants are the same inventive entity as that of Pastorekova et al. 1992, which was published less than one year before the priority date and does not constitute a statutory bar, and which therefore cannot be cited against them in the instant application.

In summary, Applicants respectfully rely upon the arguments and facts made of record in the prosecution of the instant application that Pastorekova et al. (1992) does not disclose a reproducible method of preparing the M75 Mab or any other MN-specific antibody, does not characterize the MN protein, or provide any MN amino acid sequence or MN cDNA sequence, and alone or in combination with any other prior art reference, cannot render the instantly claimed invention obvious. However, Applicants for the purposes of the instant U.S. prosecution absolutely remove the Pastorekova et al. (1992) reference from consideration as a prior art reference, pointing

out that it was published less then a year before the earliest priority date for the subject claims, and is the Applicants' own work, as evidence by the two accompanying affidavits of Appendices 1 and 2. Without Pastorekova et al. (1992), the instant rejection must collapse, as there is then no prior art reference cited with any relevance to MN, as Pastorek et al. (1994) is not part of the prior art, and Raychaudhuri et al. is only cited as an example of what was conventionally known in the prior art concerning preparing anti-idiotype antibodies. Applicants respectfully conclude by requesting that the Examiner reconsider and withdraw the subject rejection in view of the above arguments, facts and evidence.

Second 35 U.S.C. § 103(a) (Section 12 of the Office Action)

In accordance with the instructions provided by the Examiners in the telephone interview of March 7, 2005, Applicants are submitting evidence herewith that the hybridoma that secretes the G250 Mab ("G250 hybridoma") had not been deposited at an international depository under the Budapest Treaty, nor had the G250 Mab, the G250 protein or the G250 nucleic acid been characterized or identified at the earliest U.S. priority date claimed for the instant application, that is, October 21, 1992.

Claims 22, 30, 36-38, 42-43, 46-48 stand "rejected under 35 U.S.C. 103(a) as being unpatentable over Oosterwijk et al [a] (WO 88/08854) as evidenced by Uemura et al [Br. J. Cancer, 81(4): 741-746, 1999] and as evidenced by Pastorek et al [Oncogene, 9: 2877-2888, 1994] in view of Raychaudhuri et al. [J. Immunology 139(1):271-278, 1987]. . . ." [Office Action, page 13, Section 12.] The Office Action continues at pages 14-15:

> [I]f the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present. . . . **[I]t is Mab G250 taught by Oosterwijk et al [a] that is the relevant antigen for the production of an anti-idiotypic antibody**. . . . Thus, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have produced an anti-idiotype antibody to Mab G250 as a therapeutic composition for treating renal cell carcinomas.

[Final Office Action, Section 12, pages 14-15; emphasis added.]

The above quoted statements presuppose that one of skill in the art has in his or her possession the G250 Mab, a method of producing the G250 Mab reproducibly, the G250 antigen and/or the G250 cDNA. As pointed out above in describing the March 7 telephone interview, and in the arguments and facts made of record herein and in the earlier prosecution of the instant application, none of the prior art references, alone or in any

combination, and certainly not Oosterwijk et al., WO 88/08854 as will be shown in detail below by Oosterwijk et al.'s own admissions, provides sufficient information for one of skill in the art to produce reproducibly the G250 Mab or any MN-specific antibody.

As discussed at page 48 of Applicants' response to the first Office Action and as confirmed by Oosterwijk et al. (see below), the G250 hybridoma cell line was not deposited until 2001 and therefore, at the time of filing the instant invention one of skill in the art would not have been able to produce the G250 Mab reproducibly, let alone anti-idiotype antibodies to antibodies that specifically bind the MN protein. Moreover, the company, who has been working with Oosterwijk et al. on the G250 Mab, Wilex AG, dropped an opposition to Zavada et al.'s European MN patent [EP-B 0 637 336] (corresponding to the instant application's earliest U.S. priority application) in favor of taking a license under the Zavada et al. patents/applications, constituting further evidence that WO 88/08854 did not render obvious the claimed invention.

The deficiencies of Oosterwijk et al., WO 88/08854, cannot be filled by the other cited references of the instant rejection (or for that matter by any prior art reference) in that the only other cited references that concern MN are

Pastorek et al. (1994) and Uemura et al. (1999), neither of which are part of the prior art, having each been published years after the earliest U.S. priority date for the subject claims, that is, October 21, 1992. Raychaudhuri et al. (1987), although part of the prior art, was cited only to show what was conventionally known about preparing anti-idiotype antibodies at the time the claimed invention was made, and has no relation whatsoever with MN per se.

1. Oosterwijk et al. Admissions that WO 88/08854 Provided No "Informations" Concerning the G250 Mab Nor the G250 Hybridoma Other Than a General Immunization Protocol

Oosterwijk et al. filed a new G250 Mab-related application, WO 02/062972 [submitted as Appendix 3; filed February 7, 2002, with a priority date of February 7, 2001.] In Example 1 of WO 02/062972 [and of its corresponding U.S. application - U.S. 2004/0077081 A1 (published April 22, 2004)], Oosterwijk et al. admit that **WO 88/08854 provided very little information about the G250 Mab and G250 hybridoma**:

> The G250 hybridoma cell line was produced as described in Example 1 of WO88/08854. Therein a general immunization protocol is given. **Further informations** [sic], **e.g. a molecular characterization of the G250 antibody and the G250 hybridoma cell are lacking**.

[WO 02/062972, page 8, lines 18-21; emphasis added.]

Further, at page 2 of WO 02/062972, Oosterwijk et al. acknowledge:

> The production of a hybridoma cell line expressing G250 antibody was generally described in the international patent application WO88/08854 and Oosterwijk et al. (supra). As stated above, a cell homogenate from primary RCC lesions obtained from different patients and thus **an unspecific material was used as an immunogen**. Furthermore, **the hybridoma cell line had not been deposited with a recognized depository institution according to the Budapest Treaty.** Thus, **an exact reproduction of the G250 hybridoma cell line from the publically available prior art documents does not seem to be possible**.

[WO 02/062972, page 2, lines 6-15; emphasis added.]

As disclosed above by Oosterwijk et al., "**an unspecific material was used as an immunogen**" to produce the hybridoma cell line expressing G250 antibody described in international patent application WO88/08854, and "**an exact reproduction of the G250 hybridoma cell line from the publically available prior art documents does not seem to be possible**." Therefore, Oosterwijk et al. WO 88/08854 admits by those statements, and by their actions in filing a PCT application published as WO 02/062972 A2 [and as US 2004/0077081 A1] clearly admit that one of skill in the art could not have produced the G250 Mab or any other MN-

specific antibody based on the Oosterwijk et al. WO 88/08854 disclosure.

2. The G250 Hybridoma Not Deposited until September 2001

As indicated above, Oosterwijk et al. admitted that the G250 hybridoma was not deposited with an international depository under the Budapest Treaty until September 11, 2001. The European Examiner of the Oosterwijk et al. 1988 European application indicated at page 3 of the first Communication that ". . . the monoclonal antibody producing hybridomas of the application are not deposited and thereby not reproducible. . . . In this respect, the application does not fulfill the requirement of Article 83 regarding the disclosure of microorganisms as set out in Rule 28 EPC."

Oosterwijk et al. specifically admit in the PCT application WO 02/062972 [and corresponding US 2004/0077081 A1] that the "first publically available disclosure" of the G250 hybridoma and Mab was made by its September 11, 2001 deposit of the G250 hybridoma.

> Thus, the present invention relates to a hybridoma cell capable of producing a G250 monoclonal antibody. **This hybridoma cell was deposited under the Budapest Treaty for the Deposit of Microorganisms on September 11, 2001** at Deutsche Sammlung von Mikroorganismen und Zellkulturen GmbH

(DSMZ), Mascheroder Weg 1b, 38124 Braunshweig, Germany under the Accession Number DSM ACC 2526. **The deposit is the first publically available disclosure of a G250 antibody producing hybridoma cell line**.

[WO 02/062972, page 2, lines 25-32; US 2004/0077081 A1, page 1, ¶ 0008; emphasis added.]

3. Owner of the WO 88/08854 Patent Dropped Opposition to MN European Patent in Favor of License to Zavada et al. Patents/Applications

As further evidence of the non-obviousness of the claimed invention over Oosterwijk et al., alone or in combination with any other prior art reference, Applicants respectfully inform the Examiner that Wilex AG, the company listed as the Applicant on Oosterwijk et al. WO 02/062972 A2, filed an opposition to the Zavada et al. MN European patent EP-B 0 637 336, but after the instant Applicants rebutted Wilex's opposition arguments, Wilex dropped the opposition in favor of licensing rights to the relevant Zavada et al. patents/applications.

4. Combination of References: Oosterwijk et al., Uemura et al., Pastorek et al. and Raychaudhuri et al.

As indicated above, Applicants respectfully submit that the deficiencies of Oosterwijk et al. WO 88/08854 are not

corrected by any combination of Uemura et al., Pastorek et al. and Raychaudhuri et al. for the above-stated reasons. Applicants respectfully conclude that Oosterwijk et al. does not enable the G250 Mab, since neither the G250 Mab nor the G250 antigen is identified by any biochemical characteristics, but is only given a name in the cited reference WO 88/08854, and was not accompanied by a deposit of the G250 hybridoma. Without knowledge of how to reproducibly make the G250 Mab, Raychaudhuri et al. is insufficient to overcome the deficiencies of Oosterwijk et al.

The fact that years later the MN protein is shown to be identical with the G250 antigen, as reported in Uemura et al. (1999), tells one of skill in the art nothing at the time the claimed invention was made, when only insufficient and misleading information had been disclosed about the identity of the G250 antigen. Then Pastorek et al. (1994), another reference that is not part of the prior art, has no relevance as any form of evidence, as there was no link between the G250 antigen and the MN protein that could have been made by one of skill in the art at the time the claimed invention was made, based on the prior art disclosures.

Applicants respectfully request that the Examiner reconsider the instant rejection in view of the above facts, evidence and analysis, and withdraw the second 103(a) rejection.

35 U.S.C. § 103(a) (Section 13 of the Office Action)

> Claims 22, 30, 36-38, 42-43, 46-48 stand
>
> rejected under 35 U.S.C. 103(a) as being unpatentable over Oosterwijk et al (International Journal of Cancer, 38:489-494, 1986, Ids 10/19/2001) as evidenced by Uemura et al [Br. J. Cancer, 81(4): 741-746 (1999)] and as evidenced by Pastorek et al [Oncogene, 9: 2877-2888 (1994)] in view of Raychaudhuri et al [J. Immunology, 139(1): 271-278 (1987)]. . . .
>
> The response argues as above and the rebuttal to these arguments is as above. . . ."

[Office Action, page 16, Section 13.] Applicants respectfully traverse that rejection, relying on arguments presented in the previous section, noting that most of the disclosure of the Oosterwijk et al. 1986 article (International Journal of Cancer) is contained within the Oosterwijk et al. application (WO 88/08854). Applicants respectfully point out that Oosterwijk et al. 1986, the only reference not cited in the second 103(a) rejection above, does not contain any disclosure further than Oosterwijk et al. WO 88/08854, concerning how one of skill in the art would produce reproducibly the G250 Mab or any other MN-

specific antibody, or any information about how one would be able to identify the G250 protein or cDNA. Therefore, Oosterwijk et al. 1986 cannot cure the deficiencies of Oosterwijk et al. WO 88/08854, which was filed after Oosterwijk et al. 1986 was published.

There is nothing in Oosterwijk et al., alone or in combination with any other prior art reference, such as Raychaudhuri et al. (1987), that would enable "one of ordinary skill in the art . . . to make or synthesize" a MN-specific antibody, let alone the claimed anti-idiotype antibodies, which comprise an internal image corresponding to an MN protein/polypeptide epitope until after the disclosure provided in the earliest U.S. priority application for the instant application. Applicants respectfully rely on the facts, evidence and analysis provided above to overcome the instant rejection wherein Oosterwijk et al. 1986 replaces Oosterwijk et al. WO 88/08854.

In specific reference to the cited Oosterwijk et al. 1986 Int. J. Cancer article, Oosterwijk et al. WO 02/062972 stated the following:

> The production of a hybridoma cell line expressing G250 antibody was generally described in the international patent application WO88/08854 and Oosterwijk et al. (supra) [**i.e., Oosterwijk et al., Int. J.**

> **Cancer 38:489-494, 1986**]. As stated above, a cell homogenate from primary RCC lesions obtained from different patients and thus an unspecific material was used as an immunogen. Furthermore, the hybridoma cell line had not been deposited with a recognized depository institution according to the Budapest Treaty. Thus, **an exact reproduction of the G250 hybridoma cell line from the publically available prior art documents does not seem to be possible**.

[WO 02/062972, page 2, lines 7-15; emphasis added.]

According to Oosterwijk et al., prior to the 2001 priority date for WO 02/062972 A2 (and the corresponding US 2004/0077081 A1) [well after the earliest U.S. priority date claimed for the instant invention], one of skill in the art would not have been able to reproducibly make the G250 antibody from the "publically available prior art documents". Those "publically available prior art documents" would then **include** the cited Oosterwijk et al. (1996), Uemura et al. (1999), Pastorek et al. (1994) and Raychaudhuri et al. (1987) documents. That admission by Oosterwijk is further evidence of the lack of enablement provided by the cited references, even the non-prior art references, for the production of the G250 Mab.

Since nothing in Raychaudhuri et al. (1987) corrects the deficiencies in Oosterwijk et al. (1986) for the reproducible production of the G250 Mab or identification of the

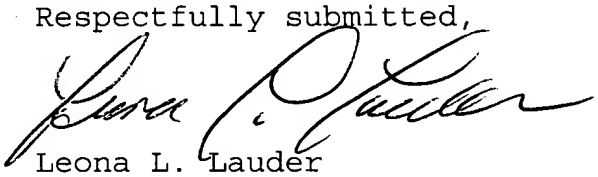
G250 antigen, and since Uemura et al. (1999) and Pastorek et al. (1994) only provide evidence published after the priority date of the instant application that the G250 antigen is identical to the MN antigen, but do not correct the deficiencies of Oosterwijk et al. 1986 for the reproducible production of the G250 Mab or identification of the G250 antigen at the time the claimed invention was made, there is nothing in the cited combination of references that would suggest or render obvious the claimed invention. One of skill in the art with the disclosure of Oosterwijk et al. 1986 and Raychaudhuri et al. (1987) at the time the claimed invention was made, could not have reproducibly made the G250 Mab or the G250 antigen by Oosterwijk et al.'s own admissions, let alone the claimed anti-idiotypic antibodies comprising an internal image corresponding to an MN protein/polypeptide epitope.

Applicants respectfully conclude neither Oosterwijk alone or as evidenced by Pastorek et al. 1994 and Uemura et al. 1999 in view of Raychaudhuri et al. renders the instantly claimed invention obvious, but instead as explained above is evidence of the nonobviousness of the instant invention. Applicants respectfully request that the Examiner reconsider the instant rejection in view of the above noted facts, evidence and analysis, and withdraw the subject third 103(a) rejection.

CONCLUSION

Applicants respectfully conclude that the claims are in condition for allowance, and earnestly request that the claims be promptly allowed. If for any reason the Examiner feels that a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to telephone the undersigned Attorney for Applicants at (415) 981-2034.

Respectfully submitted,



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Dated: April 11, 2005